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Interaction of SPEED 98 listed chemicals and their related compounds with the androgen receptor and their 3D-QSAR analysis

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In this study, we characterized androgen receptor (AR) activity of the listed chemicals by the Ministry of the Environment, Japan, so called SPEED 98 and their related chemicals based on *in vitro* reporter gene assay using MDA-kb2 human breast cells that stably express an androgen responsive luciferase reporter gene, MMTV-luc. Among 99 tested chemicals, 35 chemicals showed a pure AR antagonist activity and 13 chemicals had both AR agonist and antagonist activities. A three dimensional quantitative structure activity relationship (3D-QSAR) technique, Comparative Molecular Field Analysis (CoMFA), was used to probe the structural requirements for AR antagonist and/or agonist activities. A CoMFA model with $r^2 = 0.825$; $q^2 = 0.332$ (3 components) and $r^2 = 0.968$; $q^2 = 0.549$ (2 components) was developed using structurally diverse AR pure antagonist data set (35 compounds) and AR agonist and antagonist (13 compounds), respectively. The steric and electrostatic properties were sufficient to describe the structural requirements for AR antagonist activity.